

BIOMATERIALS

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Ca-DEFICIENT HYDROXYAPATITE POWDER FOR PRODUCING TRICALCIUM PHOSPHATE BASED CERAMICS

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The properties of Ca-deficient hydroxyapatite powder synthesized from calcium nitrate and ammonium hydrophosphate at 60°C, pH = 7, and Ca/P = 1.67, 1.61, and 1.48 are presented. After sintering at 1100°C for 6 h the phase composition of the ceramic based on these powders was represented by tricalcium phosphate (Ca/P = 1.48) or tricalcium phosphate hydroxyapatite (Ca/P = 1.67 and 1.61). The grain size of the ceramic was 100 – 1000 nm.

Key words: hydroxyapatite, tricalcium phosphate, sintering, thermal conversion of calcium phosphates.

Materials based on calcium phosphates are widely used in medicine because of their superior bioactivity and biocompatibility. The wide use of calcium phosphates for creating materials for medical use is due to the fact that the inorganic component of the bone tissue is represented by calcium phosphate, namely, hydroxyapatite $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ (HAP). The regenerative approach currently popular in medicine presupposes the use of materials capable of being resorbed during implantation, i.e., dissolving it serves as a source of components for the construction new bone tissue. One of the best known and widely used in medical practice resorbable materials is ceramic based on tricalcium phosphate $\text{Ca}_3(\text{PO}_4)_2$ (TCP) [1, 2].

There are four known polymorphic modifications of TCP whose structure is of the glaserite type $(\text{K}_3\text{Na}(\text{SO}_4)_2)$ [3]. β -TCP, which is stable at temperatures below 1120°C, is structurally similar to whitlockite (mineral with the composition $\text{Ca}_{18}(\text{Mg, Fe})_2\text{H}_2(\text{PO}_4)_{14}$), which has been found in many products of biological mineralization. It crystallizes in the rhombohedral system, space group $R\bar{3}c$, unit cell parameters $a = b = 10.439 \text{ \AA}$, $c = 37.375 \text{ \AA}$, $Z = 21$, and density 3.067 g/cm^3 . α -TCP is stable at temperatures from 1120 to 1470°C. It crystallizes in a monoclinic system, the space group is $P2_1/a$, the lattice parameters $a = 12.887 \text{ \AA}$, $b = 27.280 \text{ \AA}$, $c = 15.219 \text{ \AA}$, $\beta = 126.20^\circ$, $Z = 24$, and the density 2.863 g/cm^3 . α' -TCP is the phase that is stable at tempera-

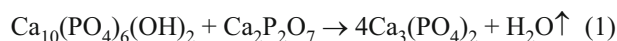
tures above 1470°C, while β' -TCP exists at high pressures [4, 5].

The interrelationship and transitions between the polymorphic modifications at normal pressure are represented by the scheme



To obtain ceramic with a fine-grain, uniform microstructure, as a rule, powders with corresponding phase composition, which are obtained by one of the chemical methods of synthesis, of which the most readily available is precipitation from water solutions, are used. A characteristic feature of TCP is that it cannot be synthesized by precipitation from solutions. α -TCP and β -TCP can be prepared by allowing components containing Ca^{2+} and $(\text{PO}_4)^{3-}$ interact in the solid phase [6].

Solid-phase synthesis of TCP (molar ratio $\text{Ca/P} = 1.5$) requires the interaction of calcium phosphates taken in prescribed quantities with ratio Ca/P less or greater than 1.5, i.e., $\text{Ca/P} < 1.5$ and $\text{Ca/P} > 1.5$. In the example presented below (reaction 1) TCP is synthesized as a result of the interaction of CPP ($\text{Ca/P} = 1$) and HAP ($\text{Ca/P} = 1.67$) in the presence of heating:



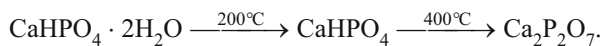
A stoichiometric mixture of the components, which corresponds to the molar ratio $\text{Ca/P} = 1.5$, is heated at tempera-

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ture 1000°C for 0.5 – 1 h to obtain the β modification and 1200°C for 0.1 – 1 h to prepare the α modification. The components of such mixtures are compounds with molar ratio $\text{Ca/P} < 1$, for example, brushite $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$, monetite CaHPO_4 , calcium pyrophosphate $\text{Ca}_2\text{P}_2\text{O}_7$ (CPP) or containing the phosphate ion, for example, $\text{NH}_4\text{H}_2\text{PO}_4$. Compounds with molar ratio $\text{Ca/P} > 1.5$ (for example, tetracalcium phosphate $\text{Ca}_4\text{P}_2\text{O}_9$, $\text{Ca/P} = 2$) or containing only the calcium ion and not the phosphate ion (for example, calcium carbonate CaCO_3 , calcium oxide CaO) are used as the components of such mixtures. The method presupposing that the components interact in the solid phase is used quite often for preparing highly dispersed α -TCP powder with binding properties. The hydrolysis of α -TCP or the acid-base interaction of α -TCP and the mixing liquid (water or water solutions of salts) are processes which occur in the production of materials for medical applications using the chemical binding technology [7].

For obtaining ceramics powders synthesized by a solid-phase method are useless because of their low activity with respect to sintering. Ceramic materials made from TCP can be obtained during sintering accompanied by a chemical reaction from powder mixtures whose components are synthesized by precipitation from solutions and are characterized by high specific surface area and small crystallite size as well as defects of the crystal lattice. For example, β -TCP ceramic has been obtained from powder mixtures HAP and CPP (RF Patent RU 2391316 C1, June 10, 2010), monetite [8] or brushite [9]. When powders of these calcium phosphates are used, the porosity of the ceramic materials increases in the series CPP – monetite – brushite. Water vapor is released when brushite and monetite are calcined, while when CPP is calcined water vapor is not released, and in the series indicated the amount of water vapor released decreases on heating. These calcium phosphates are related by a chain of transformations which occur on heating [10]:



TCP can also be obtained from amorphous calcium phosphate (ACP) and Ca-deficient HAP (Ca-dHAP), whose molar ratio Ca/P is 1.5, if the indicated phosphate is heated to temperature at least 700°C. Heat-treatment must be performed above 1200°C to prepare the α modification and in the interval 900 – 1150°C to prepare the β modification [11]. However, amorphous calcium phosphate obtained by precipitation from water solutions, as a rule, is a gel-like paste, possesses binding properties, and after drying forms a product that poorly amenable to disaggregation [12].

The structure of HAP possesses well-known mobility, i.e., its constituent ions and ion groups are tendency to undergo substitutions. Ca^{2+} can be replaced by Mg^{2+} , Zn^{2+} , and K^+ and Na^+ , the ion $(\text{PO}_4)^{3-}$ can be replaced by $(\text{CO}_3)^{2-}$, $(\text{SiO}_4)^{4-}$, and $(\text{HPO}_3)^{2-}$ and the OH group can be replaced by F, Cl, and $(\text{CO}_3)^{2-}$. A calcium deficit can be produced in

TABLE 1. Objects of Study — Calcium Phosphate Ca-dHAP Powders

Synthesis No.	Ratio Ca/P	x
1	1.67	0
2	1.61	0.36
3	1.48	1.11

the HAP structure without a substantial change of the elemental composition by replacing $(\text{PO}_4)^{3-}$ groups with $(\text{CO}_3)^{2-}$ and $(\text{HPO}_3)^{2-}$. The substitution of $(\text{CO}_3)^{2-}$ for $(\text{PO}_4)^{3-}$ virtually always occurs during HAP synthesis in air, since the presence of OH groups in solution unavoidably results in trapping of CO_2 from air by the solution, although synthesis schemes where soluble carbonates or urea are introduced into the reaction zone to regulate the degree of substitution have been described [13]. In the course of synthesis at pH close to 7, conditions are created for $(\text{HPO}_3)^{2-}$ substituting for $(\text{PO}_4)^{3-}$ in the HAP structure. In the carbonate hydroxyapatite structure charge compensation with heterovalent substitution of a carbonate ion for a phosphate ion can be achieved by a calcium deficiency and (or) sodium substituting for calcium. Charge compensation in the structure results in the formation of calcium vacancies and therefore Ca-dHAP. The effect of the ratio Ca/P on the thermal stability and sintering of HAP powders obtained in a nitrogen atmosphere with Ca/P from 1.5 to 2 and pH in the range 6.5 – 9 and temperature from 30 to 95 is examined in [14, 15]. Thus, for one fixed parameter (of a nitrogen atmosphere) three other parameters (temperature, pH, Ca/P) were varied, which made it possible to synthesize calcium phosphate powders with different ratios $\text{Ca/P} < 1.5$ to 1.71. Analyzing the data presented in [14, 15] it is evident that maintenance of Ca/P close to the prescribed value was observed at temperature above 50°C and $\text{pH} \geq 7$.

The objective of the present work was to investigate the properties of calcium phosphate powders — Ca-deficient hydroxyapatite (Ca-dHAP), and to study the microstructure of the ceramic obtained on the basis of these powders.

The Ca-dHAP powders were synthesized in air at fixed temperature (60°C) and pH (7). The ratio Ca/P in the initial solutions was 1.48, 1.61, and 1.67 (Table 1).

The calculation of the amounts of the initial salts for synthesis of Ca-deficient HAP powders was performed using the reaction



At $\text{pH} = 7.0 - 7.3$ 1 liter of a solution containing the computed amount of $(\text{NH}_4)_2\text{HPO}_4$ was added in drops at the rate 4.5 ml/min to 1 liter of a 0.5 M solution of $\text{Ca}(\text{NO}_3)_2$. The prescribed pH was maintained by adding a 25% water solution of ammonia. After the initial solutions were de-

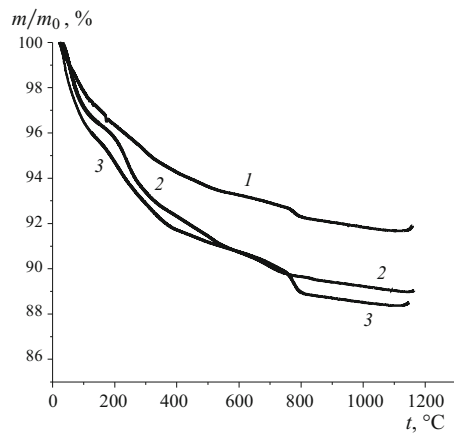


Fig. 1. Mass (m/m_0) versus temperature of Ca-dHAP powders synthesized with Ca/P: 1) 1.67; 2) 1.61; 3) 1.48.

canted the residue was allowed to stand in the mother liquor at 60°C for 20 – 30 min.

For fixed pH the formation of Ca-dHAP, which can be described by the formula $\text{Ca}_{10-x}(\text{HPO}_4)_x(\text{PO}_4)_{6-x}(\text{OH})_{2-x}$, was expected. In the process Ca-dHAP powder characterized by different deficiencies of calcium (see Table 1) was obtained.

The suspension obtained was filtered in a Büchner funnel, after which the residue was dried in 48 h at 20°C in a thin layer. Disaggregation was conducted in a planetary ball mill (Fritch) in ethyl alcohol with ratio alcohol : balls (Al_2O_3) : powder = 2 : 1 : 3 in 3 min. After disaggregation the product was dried in air for 4 h and then passed through a 200 μm sieve. The samples were pressed into $4 \times 5 \times 10$ mm rectangular bars under specific pressing pressure 50 MPa. The powders were characterized by means of XPA, SEM, DTA, and dilatometric measurements.

The XPA data (DRON-3 (Russia), CuK_α , CoK_α) shows that HAP and ammonium nitrate were present in each synthesized powder. The observed broadening of the peaks, which increases with decreasing ratio Ca/P, shows that the primary crystallites are small — 30 – 70 nm according to SEM data. After disaggregation the bulk density of the powders was 0.3 – 0.5 g/cm³.

The thermal analysis data (Perkin Elmer Pyris (USA) thermal analyzer) obtained for the powders show that a number of processes accompanied by mass loss occur (Fig. 1): removal of the adsorbed water (20 – 100°C); decomposition of

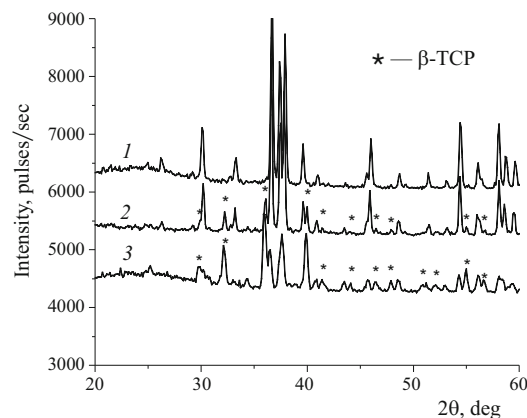
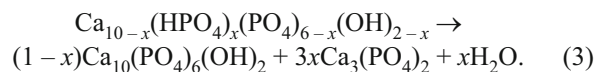


Fig. 2. XPA of a ceramic after firing at 1100°C for 6 h based on Ca-dHAP powders synthesized with Ca/P: 1) 1.67; 2) 1.61; 3) 1.48.

ammonium nitrate (50 – 220°C; according to the published data the decomposition temperature is 210°C); release of water and CO_2 from Ca-dHAP at higher temperatures. The step in the plot of the dependence of the mass on the temperature in the interval 650 – 800°C is a characteristic indicator of a calcium deficiency in HAP. The calcium deficiency is compensated by a corresponding substitute of $(\text{HPO}_4)^{2-}$ for the group $(\text{PO}_4)^{3-}$. The reaction occurring on heating in the indicated temperature interval and as a result of which HAP and TCP are formed is



Further dehydration occurs at higher temperatures (> 800°C). The dehydration depends on the water vapor pressure and results in the formation of oxyhydroxyapatite (OHAP).

In the plots presented in Fig. 1 the step indicating the presence of a calcium deficiency in the structure of the synthesized HAP is distinct only for powder synthesized with molar ratio Ca/P = 1.48. The XPA data for the samples after heat-treatment at 1100°C for 6 h (Fig. 2) attest to the presence of β -TCP in all three samples. The HAP phase is also present in the samples synthesized with Ca/P = 1.67 and 1.61. Only a calcium deficiency existing after synthesis can provide such a change of the phase composition after heat-

TABLE 2. Synthesis Conditions and Powder Characteristics

Synthesis conditions				Loss of mass at 400°C, %	Bulk density of powders, g/cm ³	Density of samples after pressing ($p = 50$ MPa), %
with (Ca^{2+}) , M	with (PO_4^{3-}) , M	Ca/P	pH			
0.5	0.3	1.67	7	5.73	0.42	40
0.5	0.3	1.61	7	7.68	0.51	43
0.5	0.3	1.48	7	8.29	0.31	39

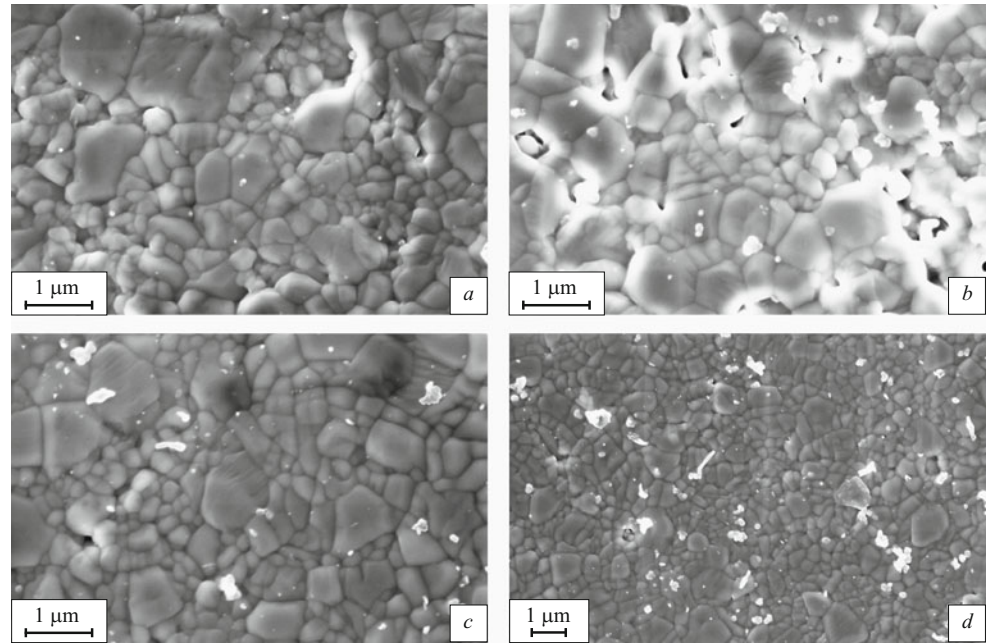
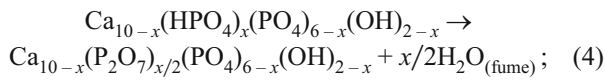


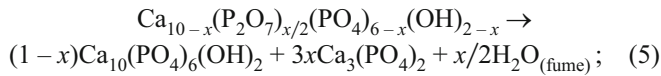
Fig. 3. Photomicrographs (sintering temperature 1100°C) obtained from powders of Ca-deficient HAP, synthesized with different ratios Ca/P: a) 1.67; b) 1.61; c, d) 1.48.

treatment. The reactions reflecting the processes occurring in the samples on heating are as follows:

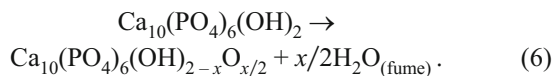
at 600°C:



at 700 – 800°C:



above 800°C:



The density of the formed samples was about 40%. In the present work the continuous shrinkage of samples based on the synthesized powders on heating was studied up to 800°C. However, no appreciable change of the length of the samples on heating up to this temperature was observed. At 800°C the linear shrinkage for all samples was 0.5 – 1.5%. The chemical reactions occurring result in the formation of calcium phosphates differing with respect to chemical composition (TCP) and structure (HAP, OHAP) from the initially present calcium phosphate (Ca-dHAP). These transformations impede the start of sintering of the powder blank at lower temperatures in contrast to the manner in which this occurs for samples made from stoichiometric HAP powders. The stoichiometric HAP powders (Ca/P = 1.67), obtained at 60°C and pH = 9, are characterized by quite high sintering activity. The shrinkage of the samples based on the stoichiometric HAP powders starts in the interval 600 – 700°C and reaches a maximum in the interval 850 – 950°C [17]. However, after sintering at 1100°C for 6 h the ceramic samples

based on this powder comprise a porous unsintered material [18].

The Ca-dHAP based samples were sintered at 1100°C. Choosing a higher temperature for sintering could give rise to a reversible phase transition of β -TCP into α -TCP, accompanied by large volume changes. After sintering at 1100°C for 6 h the density of the samples was 70 – 80% of the density of HAP (3.16 g/cm³) or β -TCP (3.067 g/cm³). Figure 3 shows a photomicrograph of the cleavage phases of a ceramic (LEO SUPRA-50VP Zeiss (Germany) scanning electron microscope). The grain size of the experimental samples lies in the interval 100 – 1000 nm with about 500 nm predominating.

In summary, the Ca-dHAP powders synthesized from water solutions at 60°C and pH = 7 can be used to obtain ceramics based on TCP, if the ratio Ca/P was 1.48 during synthesis, or the two-phase ceramic HAP/TCP, if the ratio Ca/P was 1.67 or 1.61. The occurrence of thermal conversion of Ca-dHAP into TCP and HAP shifts the start of sintering, manifested as a change of the geometric dimensions of the samples, to higher temperatures. The small size of the particles in the synthesized powder, the start of sintering at high temperatures, and the occurrence of thermal conversion all play a role in the formation of the microstructure of ceramic based on calcium phosphates with grain size not exceeding 1 μm .

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